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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 10/066,273
Filing Date: February 01, 2002
Appellant(s): ASHKENAZI ET AL.

AnneMarie Kaiser
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed August 07, 2006 appealing from the Office action mailed November 25, 2005.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The statement of the status of claims contained in the brief is correct.

(4) Status of Amendments After Final

No amendment after final has been filed.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is correct.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Evidence Relied Upon

Janknecht et al., 1995, Carcinogenesis, Vol.16, No.3, pp.443-450 ;

Herrera et al., 1996, Progress in Neurobiology, Vol.50, pp.83-107 ;

Kovacs, 1998, Neurochem. Int., Vol. 33, pp.287-97;

Coulon et al., 1999, J. Biol. Chem, Vol.274, No.43, pp.30439-46 ;

Sakurai et al., 2002, Invest. Ophthalmology and Visual Sci., Vol.43, No.8, pp.2774-81;

Otani et al., 2000, , Invest. Ophthalmology and Visual Sci., Vol.41, No.5, pp.1192-9;

Ozerdem et al., 2000, Angiogenesis, 6, pp.241-9;

Diaz-Florez et al., 1994, Histol. Histopathol., Vol.9, pp.807-43.

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 40-44 are rejected under 35 U.S.C. 101 because the claimed invention is drawn to an invention with no apparent or disclosed specific and substantial credible utility. The instant application has provided a description of an isolated protein and an antibody to this protein. The instant application does not disclose a specific biological role for these protein and antibody or their significance to a particular disease, disorder or physiological process, which one would wish to manipulate for a desired clinical effect.

It is clear from the instant application that the protein described therein is what is termed an "orphan protein" in the art.. There is little doubt that, after complete characterization, the encoded protein and the antibody that binds to the protein may be found to have a specific and substantial credible utility. This further characterization, however, is part of the act of invention and until it has been undertaken, Applicant's claimed invention is incomplete. The instant situation is directly analogous to that which was addressed in *Brenner v. Manson*, 148 U.S.P.Q. 689 (Sus. Ct, 1966), in which the court expressed the opinion that all chemical compounds are

"useful" as it appears in 35 U.S.C. § 101, which requires that an invention must have either an immediate obvious or fully disclosed "real world" utility. The court held that:

> "The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility", "[u]nless and until a process is refined and developed to this point-where specific benefit exists in currently available form-there is insufficient justification for permitting an applicant to engross what may prove to be a broad field", and "a patent is not a hunting license", "[i]t is not a reward for the search, but compensation for its successful conclusion".

The instant claims are drawn to antibodies to an isolated polypeptide of SEQ ID NO: 9 of as yet undetermined function or biological significance. It is clear from the instant specification that the novel polypeptide designated PRO444 is a secreted protein (page 3, lines 2-6 of the instant specification) that is encoded by a cDNA "DNA 26846-1397" of SEQ ID NO: 8 (page 27, lines 5-9), which "was isolated from a human fetal lung library using a trapping technique which selects for nucleotide sequences encoding secreted proteins" (page 65, lines 26-31). Clone DNA 26846-1397 was deposited with the ATCC and assigned number 203406 (page 104, lines 14-15). The research data presented in the instant specification indicate that PRO444 of SEQ ID NO: 9 induced the expression of c-fos in pericyte cells (page 142, Example 60). Based on the results of the assay disclosed in the Example 60 it was asserted that the instant PRO444 polypeptides "are useful [...] as diagnostic markers for particular types of pericyte-associated tumors" (bottom at page 142). It is also stated that the instant antibodies specific for polypeptides of SEQ ID NO: 9 are useful "for the treatment of conditions where induced angiogenesis would be beneficial including, for example, wound healing the like".

However, it is well described in the art that induction of c-fos expression represents a general cellular response to a variety of stimuli. The *c-fos* proto-oncogene is a member of the immediate-early genes (IEGs), which are rapidly induced upon stimulation of cells with growth factors, cytokines, serum or UV-light (see Janknecht et al, 1995, Introduction and p. 444, for example). In the central nervous system *c-fos* activation has been demonstrated to be induced by neurotropic factors, neurotransmitters, depolarizing agents or ion channel activating agents (Herrera et al., 1996, p. 84, first column and p. 86, second column and also Kovacs, 1998, p. 289, Mechanism of fos induction). It is summarized in Kovacs article that "[s]tereotypic inducibility of c-fos proto-oncogene rendered this cellular immediate-early gene (IEG) to be the most widely used functional anatomical mapping tool to identify cells and extended circuitries that became activated in response to various stimuli", emphasis added (page 287, first column). Thus, according to the state of the art, activation of c-fos appears to be a non-specific first line of cellular response and, therefore, one skilled in the art would readily conclude that activation of c-fos could not support the assertion that PRO444 polypeptide could be specifically used "as diagnostic marker[s] for particular types of pericyte-associated tumors". Consequently, the assertion of the utility of the claimed antibody that binds to the PRO444 polypeptide "in diagnostic assay for PRO[444], *e.g.*, detecting its expression in specific cells, tissue, or serum" (page 98, lines 24-29) or as therapeutic agents appears to be lacking evidence of record in the instant specification, as filed.

In the absence of knowledge of the biological significance of this specific PRO444 protein, there is no immediately obvious patentable use for the antibody that binds to it. According to the specification of the instant application "[A]nti-PRO antibodies are also useful

for the affinity purification of PRO from recombinant cell culture or natural sources" (page 99, lines 1-2 of the instant specification). However, because at the time of filing of the instant application the specific and substantial credible utility of the PRO444 polypeptides was not established, there appears to be no pressing practical need to use the claimed antibodies to isolate PRO444. To employ the instant PRO444 protein in the methods for generation of antibodies or diagnostic assays is not a "real world" utility because it would eventually relate to a protein for which no biological function is known. To use an antibody to polypeptide PRO444 of the instant invention in any of the disclosed methods would clearly be using it as the object of further research, which has been determined by the courts to be a utility, which, alone, does not support patentability. Since the instant specification does not disclose a substantial "real world" use for the claimed antibody to PRO444 in their currently available form, then the claimed invention is incomplete and, therefore, does not meet the requirements of 35 U.S.C. § 101 as being useful.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 40-44 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a clear asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

(10) Response to Argument

Beginning at page 4 of the Brief, Appellant summarizes case law on the utility requirement and refers to Utility Examination Guidelines (sections 1-3). Appellant further submits that "the claimed antibodies are useful in purification of PRO444 polypeptides, which in turn have utility as both therapeutic targets for tumors associated with pericytes and as stimulators of angiogenesis" (section 4, pp.7-8 of the Brief). At pages 8-10 Appellant summarizes the Examiner's arguments and states that the Examiner has not established a *Prima Facie* case that claims 40-44 lack utility (section 5-6 of the Brief). Appellant's review of the issue of utility, the case law that has been cited and the holding that is found in that case law is not disputed. Appellant's arguments have been fully considered but are not persuasive for the reasons that follow.

The asserted utility of the claimed antibodies to PRO444 polypeptides as therapeutic agents for the treatment of pericyte associated tumors is based on the results of the assay disclosed in the Example 60, which indicated that PRO444 polypeptide of SEQ ID NO: 9 induced the expression of c-fos in pericyte cells (page 142, Example 60). The state of the art with respect to the activation of *c-fos* is such that art clearly recognizes that induction of c-fos expression represents a general non-specific first line of cellular response to a variety of stimuli in a variety of cells (see articles by Janknecht et al., Herrera et al., 1996 and Kovacs, 1998 discussed above). Thus, based on the knowledge in the art, one skilled in the art would not attribute the induction of *c-fos* expression in pericytes by the instant polypeptides as a physiological reaction specifically associated to these particular polypeptides. Furthermore, the instant specification does not teach or explain the significance of *c-fos* activation in pericytes, as

a particular cell type. There are no references cited by Appellant that would support a conclusion that pericytes are the cell type, in which the *c-fos* activation has a specific and significant physiological meaning. Accordingly, one would reasonably conclude that activation of *c-fos* could not support the assertion of specific, substantial and credible utility of PRO444 antibodies as therapeutic agents for the treatment of pericyte associated tumors. Therefore, the Examiner disagrees with the Appellant's statement that "Appellants have identified a particular biological actvity of a compound and explained how that activity can be utilized in a particular therapeutic application of the compound, fulfilling the requirements for the assertion of a specific and substantial utility for the claimed invention" (top at p. 12 of the Brief).

The Declaration of Dr. Mary Gerritsen (The Gerritsen Declaration) under 37 CFR 1.132 filed January 21, 2005 is insufficient to overcome the rejection of claims 40-44 based upon lack of utility under 35 U.S.C. §§ 101 and 112, first paragraph for the following reasons.

The Gerritsen Declaration explains that retinal pericytes used in Assay 93 of Example 60 are important in regulating angiogenesis (paragraph 6 of the Declaration) and "c-fos is a transcription factor involved in the regulation of cellular growth, including cancer and angiogenesis". Therefore, "[I]n light of their significant relationship with angiogenesis and cancer, it is useful to identify compounds capable of stimulating pericytes through the c-fos pathway in order to treat, promote and diagnose these conditions" (paragraph 7 of the Declaration).

First, it is important to point out that reasoning presented in paragraphs 6 and 7 of The Declaration of Gerritsen represents only Dr. Gerritsen's own conclusions with no references to scientific publications so that the Examiner can make an independent analysis of the available

information (see *Meitzner v. Mindick,* 549 F.2d. 775, 782, 193 USPQ 17, 22 (CCPA 1977), "Argument of counsel cannot take the place of evidence lacking in the record"). As such, there appears to be no evidence presented in the instant specification, as filed, or published scientific data that would allow to correlate or specifically connect induction of *c-fos* expression with cancer or angiogenesis, as asserted in Appellant's Brief or in The Gerritsen Declaration. The art clearly recognizes that induction of *c-fos* can be evoked by a variety of extracellular stimuli, that it represents the first line of cellular response which does not require synthesis of proteins and which can be regulated at different intracellular levels (see, for example, Coulon et al., J. Biol. Chem., 1999, Vol. 274, No. 43, pp. 30439-46, abstract and page 304439 especially).

Further, as correctly pointed out in the Declaration of Gerritsen, many growth factors are capable to stimulate growth of pericytes through activation of *c-fos* pathway (paragraph 6 of the Declaration). See, for example, article by Sakurai et al. (Sakurai et al., Invest. Ophthalmology and Visual Sci., 2002, Vol. 43, No. 8, pp. 2774-81), which describes c-fos activation in pericytes treated with prostaglandins, and Otani et al. (Otani et al., Invest. Ophthalmology and Visual Sci., 2000, Vol. 41, No. 5, pp. 1192-1199), which teaches pericytic *c-fos* activation caused by angiotensin II and VEGF. Again, there appears to be no specific biological function that could be particularly attributed to PRO444 with respect to its ability to activate *c-fos* expression in pericytes.

Also, it is stated in the article published in 2003 by Ozerdem et al. (Ozerdem et al., Angiogenesis, 2003, 6, pp. 241-249), that although pericytes play important role in angiogenesis, their role in formation of tumor neovasculature is currently not fully understood and varies depending on type of tissue and tumor (see page 241, 242 and 246). Therefore, according to the

current state of the art, induction of *c-fos* expression by PRO444 cannot be specifically associated with "onset of cancer and/or angiogenesis", as asserted in the Gerritsen Declaration (paragraph 7).

At paragraph 8 of the Declaration, Dr. Gerritsen submits that activation of *c-fos* was specifically attributed to PRO444 because in Assay 93 both positive and negative controls were present. The Examiner does not dispute the correctness of the experimental protocol. It was never argued by the Examiner that there are factors that do not evoke induction of *c-fos* activation. However, there appears to be no clear physiological meaning attributed to the activation of *c-fos* by PRO444 at the time of filing. Therefore, the fact that out of 646 samples of different factors PRO444 polypeptide was among 48, which were able to induce *c-fos* expression in pericytes (paragraph 10 of the Declaration), does not, alone, provide for practical utility of the claimed antibodies. It is a matter of law that the claimed invention must be useful in currently available form, which precludes any further experimentation to establish the utility of the claimed invention. In the instant case, one skilled in the art would have to perform a significant amount of further experimentation in order to be able to use the instant claimed antibodies for diagnosis or treatment of cancer or for any other asserted use.

With respect to the issue of activation of *c-fos* and cell specificity, which was brought in paragraph 9 of the Declaration, cited earlier article by Coulon et al. clearly indicates that not only nervous cells but cells of different types response to "wide range of extracellular stimuli" by activation of immediate early response gene *c-fos* (see abstract and page 30439, for example).

At pages 12-18 of the Brief, Appellant argues that the evidence cited by the Examiner does not refute Appellant's assertion that induction of *c-fos* in pericytes is a physiological

reaction specifically induced by PRO444. Appellant's analysis of articles submitted by the Examiner has been fully considered but is not persuasive for the following reasons.

Appellant argues that article by Janknecht et al. presents data, which supports Appellant's position that activation of *c-fos* leads to induction of VEGF expression because it involves the same pathways as are involved in induction of VEGF (p.13 of the Brief). There is no argument that activation of *c-fos,* which can be achieved, according to Janknecht et al. (see introduction and p.444 specifically) by stimulation of cells with growth factors, cytokines, serum or even UV-light, can invoke variety of cellular mechanisms, many of them could be common with activation and induction of VEGF expression. However, there is no evidence of record presented in the article of Janknecht et al. to show that a compound (PRO444 polypeptide in the instant case), which is capable of stimulation of *c-fos* gene is immediately identified as a compound that also specifically induces VEGF expression or is capable of regulation of cell differentiation or proliferation, as asserted by Appellant.

Further, Appellant criticizes Herrera et al., Kovaks et al. and Coulon et al. articles as not related to pericyte activation (pages 13-14 of the Brief). The Examiner maintains that the articles were brought to support the position that *c-fos* activation is a non-specific cellular response to a variety of stimuli regardless of a cell type. Since there is no evidence in the record that pericyte represent the only cell type, in which activation of *c-fos* bears a significant physiological effect specifically associated with a clinical condition, such as cancer or angiogenesis, there appears to be no reason to conclude that limited results of activation of *c-fos* gene by PRO444 would lead to the immediate use of the antibodies that bind to PRO444 for treating that condition.

At pages 15-17 of the Brief, Appellant argues the Examiner misinterpreted the information presented in the article by Sakurai et al., and, further, that "induction of *c-fos* mRNA is an important step in the induction of VEGF expression in retinal pericytes". The Examiner maintains that information presented in publication of Sakurai et al. fully supports the Examiner's point that activation of *c-fos* is a non-specific immediate cellular response to plurality of different factors. The article by Sakurai et al. describes that expression of *c-fos* mRNA was induced by various prostaglandins (see Figure 5); however, only PGD_2 affected the expression levels of VEGF mRNA (page 2779). Thus, Sakurai et al. research demonstrated that (1) *c-fos* was induced by a variety of different PG, and (2) that one of these factors, PGD_2 induced VEGF mRNA production. Based on this result, one skilled in art would reasonably conclude that not all the factors that activate *c-fos* would necessarily induce VEGF. Furthermore, unlike in the Sakurai et al. experiments, in the instant case the only information presented in the specification, as filed, is limited to the induction of *c-fos* expression by PRO444 and no data to support the assertion that PRO444 induce VEGF expression. Finally, regarding the merit of the argument, article of Kolch et al. cited by Appellant (see pages 16-17) presents data obtained from experiments using osteoblasts, which appear to be not representative of pericytes.

Article by Otani et al. cited by the Examiner, demonstrated that angiotensin II stimulated VEGF expression on pericytes (page 1192), and that angiotensin II stimulated *c-fos* expression in pericytes (page 1195). Once again, the difference between experiments presented in the article of of Otani et al. and the instant disclosure is that Otani et al. demonstrated stimulation of VEGF expression and *c-fos* induction by angiotensin II, while in the instant case the specification discloses data regarding induction of *c-fos* by PRO444 polypeptides and hypothesizes that

PRO444 will have an effect on pericyte growth/differentiation through VEGF stimulation mechanism. There appears to be no conclusions made in Otani et al. publication to support an assertion that any factor that stimulates *c-fos* expression in pericytes also stimulates expression of VEGF. A skilled artisan, knowing that *c-fos* could be activated by many unrelated factors would readily appreciate that disclosure that PRO444 polypeptides are capable of stimulation of *c-fos* does not provide any meaningful or definitive evidence that PRO444 molecules could be used as therapeutics in treatment of pathological angiogenesis or any other clinical conditions.

At pages 18-20 of the Brief, Appellant argues that the Examiner has not established that the pericytes have no known role in angiogenesis. However, Appellant mischaracterizes the Examiner's position. To clarify, the Examiner maintains that the instant specification provides no evidence or reliance to scientific publications to support a nexus between activation of *c-fos* in pericytes and angiogenesis. The art teaches that process of angiogenesis or neovascularization is very complex and that the involvement of pericytes in angiogenesis is controversial and not fully understood (Diaz-Florez et al., Histol. Histopath., 1994, Vol. 9, pp.807-843, pages 807, 812 and 817-818 specifically). There appears to be no indication provided by Appellant or known in the art that would directly connect activation of *c-fos* in pericytes and activation/inhibition of angiogenesis. The instant specification discloses that the claimed PRO444 induces *c-fos* activation and hypothesizes that because *c-fos* is capable of inducing growth factors that induce the onset of angiogenesis, the PRO444 polypeptides can be used for stimulating angiogenesis. However, there is no disclosure that PRO444 polypeptides are involved in activation of specific pathways that lead to induction of growth factors that further induce the onset of angiogenesis, or that PRO444 are directly involved in stimulating of angiogenesis, as implied by Appellant.

Appellant argues at pages 20-21 that publication of Orlandi et al. is insufficient to support the Examiner's opinion that *c-fos* activation does not necessarily lead to VEGF stimulation. It appears that Appellant's argument ignores and contradicts the evidence presented in the art. The Examiner maintains the position that at the time of filing, no evidence that activation of *c-fos* specifically in pericytes leads to induction of VEGF was available. Appellant has not provided a single line of evidence to support a conclusion that any compound that activates *c-fos* in pericytes could be immediately useful for stimulation of angiogenesis or in any other specific way related to cancer treatment. As such, a skilled practitioner would have to resort to a substantial amount of further research to experiment and discover if PRO444 polypeptides, which were shown to induce *c-fos activation* could activate angiogenesis or have any substantial effect on pericytes growth or differentiation.

Appellant submits at pages 23-32 that the sufficient evidence of utility of the claimed antibodies was presented in the instant specification and publications of record. Appellant argues the role pf pericytes in angiogenesis at pages 24-27 and 32-33 of the Brief. First, it is important to clarify that the Examiner never disputed that pericytes have a role in angiogenesis. Anatomically, as a part of vasculature, pericytes are reasonably expected to play a significant role in formation of new blood vessels or angiogenesis, or "being involved in capillary sprouting" or any other part of the process. However, one cannot disregard the information presented in post-filing publication of Ozerdem et al., 2003, which clearly indicates that presently it is not fully understood if stimulation of pericytes results in up-regulation or down-regulation of vascularization (middle at page 8 of the Response). More importantly, the art at the time of invention does no substantiate the nexus between stimulation of c-fos in pericytes and

their involvement, positive or negative, in angiogenesis. Further, it was never argued by the Examiner that *c-fos* induction is associated with cancer or angiogenesis. As fully explained earlier, the art recognizes that *c-fos* proto-oncogene plays a role in cell differentiation and transformation and because these processes are strongly related to tumor pathology, the role of c-fos transcription factor in cancer has been closely investigated and at present is not fully established. The Examiner presented several review articles, which clearly explain that activation of immediate-early genes, such as *c-fos*, is caused by a wide variety of stimuli, not all of them limited to carcinogenesis or angiogenesis. Therefore, one skilled in the art would immediately appreciate that not every stimulus that results in activation of *c-fos* has role in cancer or angiogenesis.

At pages 27-29 and 34-35 of the Brief, Appellant argues that VEGF has an established role on promoting angiogenesis. The Examiner agrees that the role of angiogenic factor VEGF is well established. There is also no dispute that the art at the time of filing discloses that pericytes could secrete VEGF. However, there appears to be no evidence of record to show that induction of *c-fos* in pericytes is directly and specifically associated with expression of VEGF.

Appellant submits at pages 29-31 and 35-36 of the Brief that it is an established fact that *c-fos* stimulates VEGF expression. Appellant argues that because *c-fos* encodes a subunit of the nuclear transcription factor AP-1 and because AP-1 plays a role in the expression of VEGF, then *c-fos* stimulates VEGF expression. Appellant presentes articles by Tischer et al, Shima et al. and Kolch to support this argument. Appelant's arguments have been fully considered but are not persuasive because the relationship between *c-fos*, AP-1 and VEGF expression is not obvious. Appellant's reasoning lacks support in the specification as originally filed and also in the

publications of record because there appears to be no indication that induction of expression of *c-fos* protooncogene that is known to be induced by many cellular stimuli, including growth factors, cytokines, T-cell activators, UV irradiation, hypoxia and PMA (see reasoning earlier and also article Orlandi et al., 1996) leads to stimulation of VEGF expression by means of AP-1 transcription factor. On the contrary, Orlandi et al. publication discloses that, for example, in fibroblasts VEGF expression is unaffected by *c-fos*. The Examiner maintains that because activation of *c-fos* represents a general non-specific cellular response, which is not limited to any particular cell type or particularly associated with a specific physiological function, there appears to be no scientific logic to conclude that the instant PRO444 polypeptides, as inducers of *c-fos* expression, are involved in tumorgenesis, as asserted in the instant specification.

It appears that Applicant has taken the position that because PRO444 activates *c-fos* expression in pericytes (with no comparison to other cell types), and because *c-fos* plays a role in cell differentiation/ transformation, than PRO444 could be used for treatment of pericyte-associated tumors. Also, again, because PRO444 activated *c-fos* expression in pericytes, and because pericytes are the cells present in blood vessel wall, then PRO444 is associated with angiogenesis in pericyte cells. The issue, however, remains that at the time of invention, no disclosure in the form of factual data or reliance to scientific reasoning of relevance of *c-fos* activation by PRO444 polypeptides in pericytes to diagnosis or treatment of cancer in pericytes or formation of blood vessels has been presented. The fact that PRO444 polypeptides induced *c-fos* in pericytes does not provide for immediate use of PRO444 specific antibodies for treatment of cancer or for inhibition of blood vessel formation. There is little doubt that, after complete characterization of the biological role of PRO444 in *c-fos* activation, this polypeptide and

antibodies that specifically bind to it may be found to have a specific role in cancer and angiogenesis, which would support their specific and substantial credible utility. This further characterization, however, is part of the act of invention and until it has been undertaken, Applicant's claimed invention is incomplete. While an antibody that binds a polypeptide that has a stated correlation to a specific disease condition or physiological function would be considered a "substantial utility" in the context of identifying potential candidates for preventive or therapeutic measures, in the instant case the claimed antibodies are suitable only for additional research. The instant situation is directly analogous to that which was addressed in *Brenner v. Manson*, 148 U.S.P.Q. 689 (Sus. Ct, 1966), in which the court expressed the opinion that all chemical compounds are "useful" as it appears in 35 U.S.C. § 101, which requires that an invention must have either an immediate obvious or fully disclosed "real world" utility.

At pages 36-37 of the Brief, Appellant refers again to the Gerritsen Declaration filed under 37 CFR 1.132 on January 21, 2005. The Gerritsen Declaration was considered and found to be insufficient to overcome the instant rejection because it does not provide support for relationship between expression of *c-fos* in pericytes and angiogenesis. The instant specification discloses induction of expression of *c-fos* in pericytes treated with polypeptide of SEQ ID NO: 9 but discloses no evidence or sound scientific reasoning to support the asserted utility that antibodies to polypeptides of SEQ ID NO: 9 could be useful in stimulation of angiogenesis. There is no disclosure found in the instant specification or in the prior art of record that would specifically substantiate the nexus between *c-fos* activation and expression of VEGF in pericytes or between *c-fos* activation in pericytes and angiogenesis.

The U.S. Court of Appeals for the Federal Circuit recently addressed the utility requirement in the context of a claim to DNA. *See In re Fisher,* 2005 WL 2139421 (Sept. 7, 2005). The *Fisher* court interpreted *Brenner v. Manson*, 383 U.S. 519, 148 USPQ 689 (1966), as rejecting a "de minimis view of utility" 2005 WL 2139421, at *4. The *Fisher* court held that § 101 requires a utility that is both substantial and specific. *Id.* At *5. The court held that disclosing a substantial utility means "show[ing] that an invention is useful to the public as disclosed in its current form, not that it may be useful at some future date after further research. Simply put, to satisfy the 'substantial' utility requirement, an asserted use must show that the claimed invention has a significant and presently available benefit to the public." *Id.*

Just as in *Fisher* case where the Board reasoned that use of the claimed ESTs for the identification of polymorphisms is not a specific and substantial utility because "[w]ithout knowing any further information in regard to the gene represented by an EST, as here, detection of the presence or absence of a polymorphism provides the barest information in regard to genetic heritage," (*Id.,* slip op. at 15), in the instant case, in view of the absence of clear understanding of the relationship between PRO444 polypeptide of SEQ ID NO: 9 and activation of *c-fos* and also what effect this might have on angiogenesis, the instant polypeptide PRO444 is suitable only for additional research to identify or reasonably confirm a "real world" context of use. Consequently, since the polypeptide of SEQ ID NO: 9 does not have a substantial or well-established utility as a diagnostic marker or as a therapeutic target, it is unclear as to what is the specific and substantial or well established utility of an antibody which binds to a polypeptide which lacks utility.

Thus, for reasons set forth and also reasons of record in the previous communications of record, the claimed antibodies do not have a real-world use and do not meet the utility requirements under 35 U.S.C. 101.

Further, since the claimed invention is not supported by either a clear asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

For the above reasons, it is believed that the rejections should be sustained.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

Respectfully submitted,

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